Di-n-propylphthalate

CAS #131-16-8
Swiss CD-1 mice, at 1.25, 2.50, and 5.00% in feed
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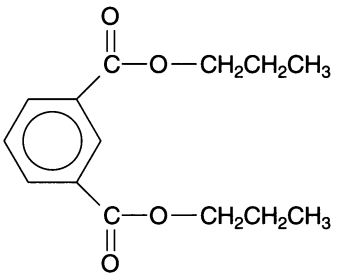

Di-n-propylphthalate (DPrP) was tested using the RACB protocol in Swiss CD-1 mice as part of a structure–activity evaluation of a variety of phthalates (Heindel et al., Fundam Appl Toxicol 12:508–518 [1989]). Body weights, food and water consumptions, and clinical signs in a dose-range-finding study were used to set doses for the main study of 0.0, 1.25, 2.50, and 5.00% in feed. Based on measured feed consumption (which was not reduced by DPrP exposure), these concentrations produced calculated consumption estimates of approximately 1.9, 4.06, and 8.63 g/kg/day.

Over the course of Task 2 (the continuous breeding phase of the study), male mice gained an average of 15, 7, 5, and 2% of their prestart body weight in the control to high dose group, respectively. The seven deaths studied were distributed among the groups and were not attributed to DPrP exposure. While there were no adverse reproductive effects observed at the low dose, there was a 44% reduction in the number of live pups per litter in the middle dose group and an 8% reduction in live pup weight adjusted for litter size. The high dose group was sterile; no high dose pairs had any pups.

These significant reproductive effects prompted a crossover mating trial to determine the affected sex, using the control and 5% dose groups. This was performed after the last litter was weaned for F_1 fertility evaluation. While equal proportions of the groups showed evidence of mating, none of the treated females bore any young when bred to control males. Litters from treated males were 34% smaller than those from control males; pup body weights were unchanged.

After the crossover mating and delivery, the control and high dose F_0 mice were killed and necropsied. Treated females weighed 14% less than controls, while liver weight and kidney weights, adjusted for body weight, were 185 and 86% of control values, respectively. Terminal male body weights were 15% less than controls, while adjusted liver weights were 61% greater. Adjusted weights of kidneys, seminal vesicles, epididymis, and prostate were reduced by 22, 24, 20, and 20%, respectively. Absolute testis weight was reduced by 36%. Sperm count was reduced by 41%, sperm motility by 8%, and sperm abnormalities were elevated by 51%.

Although there was significant liver weight increase and the livers of treated animals appeared darker at necropsy, there were no hepatic changes noted microscopically. Major microscopic findings were limited to testicular atrophy and associated epididymal effects.

An evaluation of the second generation was not conducted.

In summary, di-n-propylphthalate caused reproductive toxicity at doses that reduced parental weight gain. Both sexes were affected, based on fertility performance and necropsy findings of the high dose group.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB85247856/AS**
Chemical: **Di-n-propylphthalate**
CAS#: **131-16-8**
Mode of exposure: **Feed**
Species/strain: **Swiss CD-1 mice**

F_0 generation — Dose concentration →	1.25%	2.50%	5.00%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, —	↓, ↓	↓, ↓
Kidney weight[a]	•	•	↓, ↓
Liver weight[a]	•	•	↑, ↑
Mortality	—, —	—, —	—, —
Feed consumption	—, —	—, —	—, —
Water consumption	•	•	•
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
x̄ litters/pair	—	—	↓
# live pups/litter; pup wt./litter	—, —	↓, ↓	↓, ↓
Cumulative days to litter	—	—	•
Absolute testis, epididymis weight[a]	•	•	↓, ↓
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	↓, ↓
Epidid. sperm parameters (#, motility, morphology)	•	•	↓, ↓, ↑
Estrous cycle length	•	•	—

Determination of affected sex (crossover)	Male	Female	Both
Dose level	—	5%	—

F_1 generation — Dose concentration →	1.25%	2.50%	5.00%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	•	•	•
Mortality	•	•	•
Adult body weight	•	•	•
Kidney weight[a]	•	•	•
Liver weight[a]	•	•	•
Feed consumption	•	•	•
Water consumption	•	•	•
Clinical signs	•	•	•
Reproductive toxicity			
Fertility index	•	•	•
# live pups/litter; pup wt./litter	•	•	•
Absolute testis, epididymis weight[a]	•	•	•
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	•
Epidid. sperm parameters (#, motility, morphology)	•	•	•
Estrous cycle length	•	•	•

Summary information	
Affected sex?	Female
Study confounders:	None
NOAEL reproductive toxicity:	1.25%
NOAEL general toxicity:	1.25%
F_1 more sensitive than F_0?	Unclear
Postnatal toxicity:	No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.